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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/870,937	05/30/2001	Bin Wu	PP-01623.002	8716

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Chiron Corporation
Intellectual Property
P. O. Box 8097
Emeryville, CA 94662-8097

EXAMINER
LAMBERTSON, DAVID A

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 05/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/870,937	WU ET AL.	
	Examiner	Art Unit	
	David A. Lambertson	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-26* is/are pending in the application.

4a) Of the above claim(s) *6-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5 and 20-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 May 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-5 and 20-26 as they read on SEQ ID NO: 1, in Paper No. 10 is acknowledged. The traversal is on the ground(s) that it would not entail an undue burden on the Examiner to search multiple polynucleotide sequences. This is not found persuasive because the burden regarding a search of multiple sequences is clearly established by the fact that each individual sequence is chemically distinct, thereby conferring a different structure-function relationship for each sequence. Furthermore, it was clearly set forth in the election/restriction requirement that, "[T]he Commissioner has partially waived the requirements of 37 C.F.R. 1.141 and will permit a reasonable number of such nucleotide sequences to be claimed in a single application. Under this policy, a single independent and distinct nucleotide sequence will be examined in a single application." Therefore the guidelines provided for the search of multiple polynucleotide sequences also set forth that a search of multiple sequences results in a search burden.

The requirement is still deemed proper and is therefore made FINAL.

It is noted in applicant's reply that they have elected the *species* SEQ ID NO: 1 to be searched. Applicant is reminded that there was no species election requirement in the previous Office Action, and that each SEQ ID NO represents a distinct *invention.* As such, only SEQ ID NO: 1 will be searched as the elected invention.

Claims 1 and 3-26 are pending in the application. Claims 6-19 are withdrawn from consideration as being drawn to non-elected inventions.

Priority

Applicant's claim for domestic priority to US Application No. 60/208,435 under 35 U.S.C. 119(e) is acknowledged.

Information Disclosure Statement

The information disclosure statement filed August 30, 2001 as Paper No. 6 has been considered, and a signed and initialed copy of the PTO-1449 form is attached to this Office Action.

Drawings

New corrected drawings are required in this application because of the reasons set forth in the attached Draftsperson's review (form PTO-948). Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Claim Objections

Claims 20-26 are objected to as being drawn to non-elected embodiments. Specifically, the claims read on non-antisense inhibitors of KIAA0175.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-5 and 20-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims any antisense inhibitor of KIAA0175 in the form of an isolated antisense molecule or a pharmaceutical composition comprising one or two such molecules. The claims read on a broad genus of antisense molecules with the capacity to act as antisense inhibitors of KIAA0175.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicants were in possession of the claimed genus. In the instant case, the specification does not sufficiently describe a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, to allow the skilled artisan to envision the claimed invention.

Applicant claims an antisense molecule or pharmaceutical composition comprising such an antisense molecule that is designed to inhibit the function of KIAA0175 by function only,

without any disclosed or known correlation between the elements and their function. In order to meet the functional limitation of the claim, that the molecule is an inhibitor of KIAA0175, the skilled artisan must be able to envision what molecules will indeed inhibit the function of KIAA0175. The specification only provides teachings regarding a few specific antisense molecules, represented by SEQ ID NO: 1, 3 and 5. Importantly, the specification does not teach that specific fragments of SEQ ID NO: 1, 3 and 5 have antisense properties, only that the full length sequences have antisense activity; this relates to claims 5 and 20, where the claims recite, "wherein said antisense molecule comprises *a* sequence of SEQ ID NO: 1", thereby implying that smaller fragments of SEQ ID NO: 1 have antisense activity towards KIAA0175. The specification does not teach what common structural features of these molecules, or smaller fragments thereof, have the capacity to act as inhibitors of KIAA0175, therefore the representative number of species described does not describe the genus that is claimed. For example, the skilled artisan cannot envision what molecules (e.g., what 17 nucleotides corresponding to SEQ ID NO: 9) will hybridize specifically to exposed portions of the KIAA0175 gene such that the gene is inhibited, or what molecules will not exhibit non-antisense effects (as described by Branch in *TIBS* **23**: 45-50, 1998; see entire document, for example page 45, middle column and page 46, the paragraph bridging the left and middle columns). Similarly, the skilled artisan cannot envision what smaller fragments of SEQ ID NO: 1, for example, would display the antisense activity that the full length sequence of SEQ ID NO: 1 displays because there is no description of what structural features or particular sequences within SEQ ID NO: 1 are required for such activity. As a result, the skilled artisan cannot envision a sufficient number

of embodiments of the instant invention from the instant specification to see that the inventor was in possession of the claimed invention.

The prior art does not provide sufficient information on the subject to overcome the deficiencies of the instant specification. There is no description in the prior art that allows one to envision a representative number of antisense KIAA0175 inhibitors, either by disclosing a representative number of KIAA0175 antisense molecules or by disclosing structure-function features of the molecules, so that one of skill in the art could envision the claimed invention. To the contrary, the prior art (see for example the Branch review cited above) indicates how a good antisense molecule requires careful design and forethought to produce the desired effect. As a result, the skilled artisan cannot rely on the prior art to envision a sufficient number of embodiments of the instant invention to see that the applicant was in possession of the claimed genus.

Neither the specification of the instant application or the prior art teaches a structure-function relationship for a representative number of antisense KIAA0175 inhibitors so as to adequately describe the claimed genus. As a result, the skilled artisan would not be able to envision the claimed invention by relying on the teachings of the prior art or the instant specification. Therefore applicant has not satisfied the written description requirement to show the skilled artisan that they were in possession of the claimed genus.

Claims 20-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims a composition comprising a therapeutically effective amount of at least one KIAA0175 inhibitor, wherein at least one of said KIAA0175 inhibitor is an antisense molecule. The claims read on a broad genus of compositions comprising any number of KIAA0175 inhibitors, some of which may not be antisense molecules because there may be a number of KIAA0175 inhibitors in the composition, only one of which needs to be an antisense molecule.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicants were in possession of the claimed genus. In the instant case, the specification does not sufficiently describe a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics.

Applicant claims KIAA0175 inhibitors by function only, without any disclosed or known correlation between the elements and their function. The specification only provides teachings regarding the use of specific antisense molecules (SEQ ID NO: 1, 3 and 5) to inhibit the function of KIAA0175. The specification does not describe what other molecules have the function of inhibiting KIAA0175 function, nor does the specification describe what properties of a given molecule would allow the skilled artisan to envision its use as an inhibitor of KIAA0175

function. Thus, the skilled artisan cannot envision a sufficient number of embodiments of the claimed invention from the instant specification because the specification only discloses the features of three specific antisense inhibitors, and does not describe non-antisense inhibitors that can be used in the compositions of the invention.

The prior art does not provide sufficient information on the subject to overcome the deficiencies of the instant specification. There is no description in the prior art that allows one to envision a representative number of non-antisense molecules, or even antisense molecules other than SEQ ID NO: 1, 3 and 5, by disclosing the relevant structural or functional properties of KIAA0175 inhibitors so that one of skill in the art could envision the claimed invention. Thus the skilled artisan cannot rely on the prior art to envision a sufficient number of embodiments of the instant invention to see that the applicant was in possession of the claimed genus.

Neither the specification of the instant application or the prior art teaches a structure-function relationship for a representative number of KIAA0175 inhibitors. As a result, the skilled artisan would not be able to envision the claimed invention by relying on the teachings of the prior art or the instant specification. Therefore applicant has not satisfied the written description requirement to show the skilled artisan that they were in possession of the claimed genus.

Claims 1, 3-5 and 20-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (*United States v. Telectronics.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based upon a single factor but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following:

Nature of the invention. The nature of the invention is a genus of isolated antisense molecules that are capable of inhibiting the function of KIAA0175, as well as a pharmaceutical composition, comprising one or more such antisense molecules, that is capable of inhibiting the function of KIAA0175. The asserted use of these molecules/compositions is as a therapeutic composition, which reads on antisense gene therapy techniques.

Scope of the invention. The scope of the invention is very broad, encompassing a broad genus of molecules that includes any and all KIAA0175 antisense molecules, as well as non-antisense inhibitors (See specifically claim 20). The specification, however, only identifies antisense molecules that are inhibitors of KIAA0175, specifically a few species of the claimed genus of antisense molecules (SEQ ID NOS: 1, 3 and 5) without any indication of what features or smaller fragments of the molecules confer the claimed function, the inhibition of KIAA0175. The skilled artisan cannot determine which antisense molecules within this broad scope will be able to hybridize successfully to the KIAA0175 gene or which antisense molecules will have detrimental "non-antisense effects" when used, which are issues that remain a problem in antisense therapy techniques (for a review, see Branch *TIBS* **23**: 45-50, 1998, as recited above).

State of the art. The state of the art as it regards antisense gene therapy, in general, indicates that the therapeutic applications contain numerous pitfalls. First, the design of the antisense molecule requires consideration of both "non-antisense effects" and the "internal structures of the target RNAs and their associations with other proteins," (Branch, *TIBS* **23**: 45-50, 1998; see the entire document, for example page 45, middle and right columns). In addition, additional considerations such as RNA site selection, delivery of the antisense molecule, and maintaining the antisense molecule at the target site must be taken into account (Jen *et al. Stem Cells* **18**: 307-319, 2000; see for example the Abstract, last paragraph, and page 313-314, the section entitled "Application of the Antisense Strategy"). Finally, gene therapy, whether it is for the delivery of a coding sequence, or in this instance an antisense-expressing vector, contains numerous deficiencies surrounding its efficacy. For example, the review by Mountain indicates that "developing effective gene therapies is technically much more demanding than originally anticipated, and that the first generation of vectors gave inadequate performance in several respects that are important for achieving clinical benefit" (*TIBTECH* **18**: 119-128, 2000; see entire document, for example page 120, first full paragraph, right column).

Improvements are required for the vectors used for gene therapy, including specificity and efficacy of transfer and duration of expression of the therapeutic polynucleotide (e.g., an antisense molecule) (see for example, *TIBTECH* **18**: 119-128, 2000, page 121, second full paragraph, left column), each of which is required to use the claimed invention. When consulting the prior art in order to use the claimed invention with respect to the particular KIAA0175 antisense molecules/pharmaceutical compounds, the skilled artisan would encounter

these deficiencies with regard to antisense gene therapy, thereby requiring additional teachings other than those in the prior art in order to use the invention.

Number of working examples and Guidance provided by applicant. Confronted with the deficiencies associated with antisense gene therapy present in the prior art, the skilled artisan would consult the instant specification to overcome these deficiencies in order to use the claimed invention. However, the instant specification provides only three individual KIAA0175 antisense molecules, without enabling smaller fragments of these molecules that exhibit antisense activity, and without enabling non-antisense inhibitors of KIAA0175. Although the specific antisense molecules that are described in the specification (SEQ ID NO: 1, 3 and 5) have been shown to inhibit KIAA0175 activity in cells *in vitro*, there is no nexus provided for their use as a therapeutic composition in an organism, which is the asserted use of the invention. As a result, the skilled artisan would not be able to make and use the claimed invention along its asserted real-world use in light of the teachings of the instant specification.

Level of skill in the art. Although the concept of antisense gene therapy is simplistic in theory, the application of this technology in an asserted real-world fashion has many shortcomings. When considering the deficiencies for antisense gene therapy in the prior art (see above), and the fact that the instant specification does not overcome these shortcomings, the level of skill in the art as it concerns antisense gene therapy techniques is highly underdeveloped.

Unpredictability of the art. The art is highly unpredictable, both in terms of the broad scope of functionally active KIAA0175 antisense molecules, and in terms of the use of antisense technologies as part of a therapeutic approach. First, no structure-function relationship has been provided with respect to the molecules themselves, thus the skilled artisan would be required to

practice undue, unpredictable trial and error experimentation in order to determine which antisense molecules would have the ability to act as KIAA0175 inhibitors (e.g., which molecules are effective therapeutically while not giving non-antisense effects, etc.). Second, as supported above by the state of the art, antisense gene therapy is in itself unpredictable in practical use. For example, the skilled artisan cannot determine how to adequately express the proper antisense molecule in the proper cell of an organism for an appropriate duration of time so as to achieve a selective, therapeutic effect. The instant specification has not overcome the deficiencies in the art that are described in the prior art, therefore the skilled artisan would not be apprised as to how to use the invention as a therapeutic. The lack of a structure-function relationship for the genus of molecules that are claimed, combined with the deficiencies set forth in the prior art and a lack of teachings in the instant specification, indicates that the skilled artisan would have to practice undue, unpredictable trial and error experimentation when using the claimed invention.

In conclusion, a tremendous amount of experimentation is required in order to make and use the claimed invention. The skilled artisan would be required to make a determination of what antisense molecules are functional for inhibiting the activity of KIAA0175 in an in vivo, therapeutic environment. The skilled artisan would then have to determine what parameters are necessary in order to overcome the deficiencies of antisense gene therapy for the specific case of each individual KIAA0175 antisense molecule. AS a result, the instant specification has not enabled the skilled artisan to make and use the claimed invention as it regards its asserted utility.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claim 5 is dependent on cancelled claim 2, therefore the claim is indefinite because it is unclear what limitations apply to claim 5.

Allowable Subject Matter

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (703) 308-8365. The examiner can normally be reached on 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David A. Lambertson
May 5, 2003

PATENT EXAMINER
Gerald G. Leffler
A.U. 1636